(9)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

TXR No. 0051571

MEMORANDUM

Date: 13-FEB-2003

Subject: **IMIDACLOPRID; Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Decision Document.** DP Barcode D287400. Chemical 129099. Case 294718. Submission S609879.

From: Jennifer Tyler, Chemist, Registration Action Branch 1 (RAB1)/HED (7509C)
David Nixon, Toxicologist, RAB1/HED (7509C)

Through: Christine Olinger, HED MARC Chair (7509C)
G. Jeffrey Herndon, Branch Senior Scientist, RAB1/HED (7509C)

To: Yan Donovan, HED MARC Executive Secretary (7509C)

Introduction

The HED MARC met on 12/18/02 to discuss the imidacloprid degradates of concern in drinking water only. Residues of concern in plants and livestock were determined in a meeting of the Metabolism Committee on 6/22/93 (Memo, D. Griffith, No DP Barcode). The questions posed to the MARC by the imidacloprid risk assessment team were as follows:

- Is there any scientific objection to conducting the drinking water assessment for imidacloprid in terms of imidacloprid *per se*?
- Are additional imidacloprid degradates of special toxicological concern? If so, which one(s)? Do they warrant inclusion in the drinking water assessment?

Material Reviewed

RAB1 submitted a briefing document prepared by Jennifer Tyler and David Nixon (Memo, 12/18/02, D287025). The Evironmental Fate and Effects Division (EFED) submitted a drinking water briefing document prepared by Michael Barrett to the MARC electronically on 12/16/02. No additional documents were presented at the meeting.

MARC Members in Attendance: Abdallah Khasawinah, Alberto Protzel, Christine Olinger, Yan Donovan, Norman Birchfield, Rick Loranger, Leung Cheng , David Nixon, John Doherty

MARC Members in Absentia: Bill Wassell, Sheila Piper, Leonard Keifer, Steve Knizner

non-MARC Members in Attendance: Jennifer Tyler, Jeff Herndon, Michael Barrett

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

TXR No. 0051571

MEMORANDUM

Date: 13-FEB-2003

Subject: **IMIDACLOPRID; Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Decision Document.** DP Barcode D287400. Chemical 129099. Case 294718. Submission S609879.

From: Jennifer Tyler, Chemist, Registration Action Branch 1 (RAB1)/HED (7509C)
David Nixon, Toxicologist, RAB1/HED (7509C)

Through: Christine Olinger, HED MARC Chair (7509C)
G. Jeffrey Herndon, Branch Senior Scientist, RAB1/HED (7509C)

To: Yan Donovan, HED MARC Executive Secretary (7509C)

Introduction

The HED MARC met on 12/18/02 to discuss the imidacloprid degradates of concern in drinking water only. Residues of concern in plants and livestock were determined in a meeting of the Metabolism Committee on 6/22/93 (Memo, D. Griffith, No DP Barcode). The questions posed to the MARC by the imidacloprid risk assessment team were as follows:

- Is there any scientific objection to conducting the drinking water assessment for imidacloprid in terms of imidacloprid *per se*?
- Are additional imidacloprid degradates of special toxicological concern? If so, which one(s)? Do they warrant inclusion in the drinking water assessment?

Material Reviewed

RAB1 submitted a briefing document prepared by Jennifer Tyler and David Nixon (Memo, 12/18/02, D287025). The Evironmental Fate and Effects Division (EFED) submitted a drinking water briefing document prepared by Michael Barrett to the MARC electronically on 12/16/02. No additional documents were presented at the meeting.

MARC Members in Attendance: Abdallah Khasawinah, Alberto Protzel, Christine Olinger, Yan Donovan, Norman Birchfield, Rick Loranger, Leung Cheng , David Nixon, John Doherty

MARC Members in Absentia: Bill Wassell, Sheila Piper, Leonard Keifer, Steve Knizner

non-MARC Members in Attendance: Jennifer Tyler, Jeff Herndon, Michael Barrett

MARC Decision Table

The recommendations for degradates to be included in the drinking water assessment are summarized in Table 1. The previously determined residues of concern in plant and livestock to be included in both dietary risk assessment and tolerance expression are included in Table 1 for informational purposes.

Table 1. Summary of MARC Decisions for Imidacloprid (MARC Meeting 12/18/02)

Matrix	For Risk Assessment	For Tolerance Expression
Plants	Imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent[1]	
Livestock	Imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent[1]	
Rotational Crops	Imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent[1]	
Water	Imidacloprid, Imidacloprid urea, Imidacloprid guanidine, Imidacloprid olefin	NA[2]

[1] As stated in 40 CFR §180.472.
[2] NA = Not Applicable.
Note: the chemical names and structures for these metabolites and degradates may be found in Attachment 1.

MARC Decision Rationale

Drinking Water: Environmental fate data suggest that imidacloprid is rapidly transformed under anaerobic conditions, and is particularly photolabile in water. In an aqueous photolysis study, three degradates (urea, guanidine, and olefin) were found at levels >10% of the applied dose in 2 hours. The combined residue level of these three degradates, which are likely to be found in surface water, is >40%. Judging from the structures, these degradates, which all have weaker electron withdrawing groups than the parent, are likely to be of lower toxicity than the parent, particularly from the neurotoxicity perspective. This is because a strong electron withdrawing group is thought to be related to the affinity of the chemical to the acetylcholine receptor (I. Yamamoto "Nicotine and Nicotinoids: 1962 to 1997" in *Nicotinoid Insecticides and the Nicotinic Acetylcholine Receptor*, I. Yamamoto and J.E. Casida eds, Springer-Verlag Tokyo Berlin Heidelberg New York, 1999, p. 23.). However, there is not enough toxicological information to exclude these three degradates from the drinking water assessment. Therefore, MARC recommended that for risk assessment (especially surface water), the degradates of concern should be parent and the three degradates: imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin.

Available environmental fate data also suggest that imidacloprid is stable to hydrolysis, and typically persists for many months in soil. Therefore, the parent will likely be the major residue in ground water. However, in an anaerobic aquatic study, the guanidine metabolite was found at 66% of the applied dose at day 300, indicating a potential for significant exposure to guanidine in ground water. MARC concluded that the risk assessment team should further investigate the ground water literature and imidacloprid database to determine whether the degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin) are likely to reach ground water. If so, the degradates should be included in the ground water assessment.

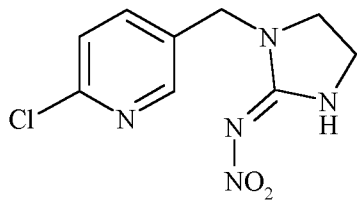
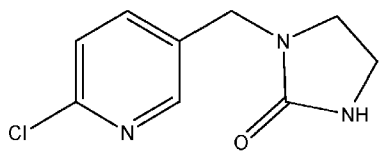
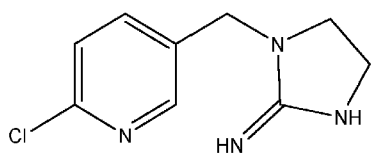
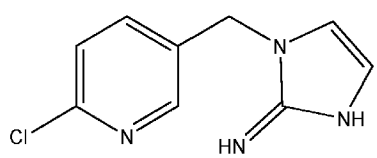
Follow-up

After the MARC meeting EFED provided revised, Tier 1 estimated environmental concentration (EECs) for ground water [Screening Concentration in Ground Water (SCI-GROW)] and surface water [FQPA Index Reservoir Screening Tool(FIRST)] for 1) the parent only and 2) the parent and total degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin). In the absence of definitive data on the persistence and mobility of these degradates, the total residues were modeled using tentatively identified total residue data from aerobic soil metabolism studies, and then assuming that the partitioning of all residues was at the same degree as imidacloprid parent. Degradate persistence and mobility data (especially from aerobic soil metabolism and batch equilibrium adsorption / desorption studies) are needed to more accurately model the total residues. However, EFED does not expect these to be exceeded under real-world usage conditions.

Modeling of total residues using the limited available data on degradate persistence and mobility results in only modest increases over the surface and ground water EECs than with parent alone. Therefore, the risk assessment team will use the surface and ground water EEC for parent and total degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin).

Reference: MARC briefing document - J. Tyler and D. Nixon, D287025, 12/18/02
cc (w/ attachments): J. Tyler, M. Barrett (EFED 7507C), R. Forrest/S. Brothers and M. Laws/D. Daniel (RD 7505C)
RDI: MARC (1/7/03), RAB1 Chemists (1/16/03), G. Herndon (2/10/03)
J.Tyler: 809B: CM#2: (703)305-5564: 7509C: RAB1

Attachment 1: Chemical Structures

Name	Structure
Imidacloprid 1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine	
Imidacloprid urea 1-[(6-chloro-3-pyridinyl)methyl]-2-imidazolidinoe	
Imidacloprid guanidine (WAK 4140) 1-[(6-chloro-3-pyridinyl)methyl]-4,5-dihydro-1H-imidazol-2-amine	
Imidacloprid olefin (WAK 3745) 1-[(6-chloro-3-pyridinyl)methyl]-4,5-dihydro-1H-imidazol-2H-imidazol-2-imine	
6-CNA 6-chloronicotinic acid